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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,875	01/16/2004	Michael L. Weiner	034405-013	6570

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EXAMINER	
BERTAGNA, ANGELA MARIE	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/758,875	WEINER ET AL.	
	Examiner	Art Unit	
	Angela Bertagna	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) *9-31 and 47-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 32-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/25/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-8 and 32-46, in the reply filed on May 11, 2006 is acknowledged.

Claims 9-31 and 47-63 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 11, 2006.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35

U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/184,120, filed 2/18/2000, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. This provisional application appears to be directed to computational methods for analyzing nucleic acids, and does not describe the nanoparticle-based nucleic acid assemblies of claims 1-8 or the dendrimer detection complexes of claims 32-46 of the instant application. The only mention of nanostructures appears on page 58 and does not provide adequate support for the instant claims. Therefore, the instant application has not been granted benefit of the earlier filing date of the above provisional application, and an effective filing date of February 17, 2001 (filing date of PCT/US01/05139) has been used.

Specification

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Specifically, the abstract uses the legal phraseology "means", for example, "means for introducing energy into the first nanoparticle."
Appropriate correction is required.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1 and 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Mirkin et al. (Nature (1996) 382: 607-609).

Regarding claim 1, Mirkin teaches a detection device comprised of a hybrid nucleic acid assembly (Figure 1). The hybrid nucleic acid assembly taught in Figure 1 of Mirkin comprises a nucleic acid polymer and a first and second nanoparticle conjugated to the nucleic acid polymer. Specifically, the first and second nanoparticles are conjugated to the nucleic acid polymer via the "linking DNA duplex". This double-stranded DNA molecule has two "sticky ends" that hybridize to the oligonucleotides immobilized on the two nanoparticles, thereby conjugating the nanoparticles (see Figure 1 and also page 608). Note that the specification does not require that the conjugation be covalent, and therefore, the assembly of Mirkin is a conjugated system. The oligonucleotide-functionalized gold nanoparticles of Mirkin comprise a means for introducing energy into the first nanoparticle and a means for detecting energy from the second nanoparticle, because upon conjugation of first and second nanoparticles via hybridization with the duplex DNA, an absorbance transition (red to purple) occurs (see page 608 and Figure 2). Therefore,

the nanoparticle-DNA hybrid assembly contains (within itself) a means for introducing energy (light) and detecting energy. Finally, the hybrid assembly taught by Mirkin includes a means for determining a physical property of the nucleic acid polymer, because since the above color change only occurs upon hybridization of the duplex linker to the complementary nanoparticle-immobilized oligonucleotides, observation of the color change is indicative of a physical property of the nucleic acid polymer, namely that it has hybridized to the functionalized nanoparticles.

Regarding claims 3 and 4, Mirkin teaches gold nanoparticles (see Figure 1 and page 607, column 2).

Regarding claim 5, formation of the assembly taught by Mirkin produces a mechanical property (a change in the flexibility of the duplex linker DNA). The images acquired using transmission electron microscopy (TEM) of the nucleic acid assembly provided information about this mechanical property of the nucleic acid polymer (page 608, column 2).

6. Claims 1 and 3-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Bamdad (US 2002/0098526 A1).

Regarding claim 1, Bamdad teaches a detection device comprising a hybrid nucleic acid assembly (paragraph 6 and Figure 1). The hybrid assembly comprises a nucleic acid polymer conjugated to a first and second nanoparticle (see Figures 5 & 6 and paragraphs 90-91, or alternatively, Example 2 on page 13). Bamdad also teaches covalent attachment mechanisms (paragraph 59). The hybrid assembly of Bamdad further comprises a means for introducing energy to the first nanoparticle and means for detecting energy from the second nanoparticle,

because upon conjugation of first and second nanoparticles via hybridization of the complementary DNA strands, an absorbance transition (red to purple) occurs (paragraphs 112-113). Therefore, the nanoparticle-DNA hybrid assembly contains (within itself) a means for introducing energy (light) and detecting energy. Finally, the hybrid assembly taught by Bamdad includes a means for determining a physical property of the nucleic acid polymer, because since the above color change only occurs upon hybridization of complementary DNA nanoparticle-immobilized DNA strands, observation of the color change is indicative of a physical property of the nucleic acid polymer, namely that it has hybridized to the functionalized nanoparticles.

Regarding claims 3 and 4, Bamdad teaches that the first and second nanoparticles may be gold (Example 2, paragraphs 109-113).

Regarding claim 5, Bamdad teaches that the assembly may function as a biosensor, where changes in mechanical properties such as flow rate, pressure and/or electroosmotic forces are measured and related to a physical property of the nucleic acid polymer, namely its ability to hybridize to a test sample (paragraphs 84-87, in particular paragraphs 86-87).

7. Claims 1, 3, and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by Dubertret et al. (US 2004/0002089 A1).

Regarding claims 1 and 3, Dubertret teaches a detection device comprising a hybrid nucleic acid assembly (see abstract and Figure 1b). The hybrid nucleic acid assembly of Dubertret comprises a nucleic acid polymer covalently linked to two nanoparticles (see Figure 1b). Dubertret teaches that the first nanoparticle may be a gold nanoparticle (Figure 1b; paragraph 10) and that the second nanoparticle may be a luminescent quantum dot (Figure 1b;

paragraph 12). The hybrid assembly of Dubertret includes a means for introducing energy to the first nanoparticle and a means for detecting energy from the second nanoparticle (paragraphs 17 & 38 teach applying fluorescence energy to both nanoparticles and detection of the change in the signal emitted from the second particle). The information gained by the change in fluorescence of the second nanoparticle provides a means of determining a physical property of the nucleic acid polymer, specifically its ability to hybridize with an added binding partner (paragraphs 17 and 38).

Regarding claim 5, the hybrid assembly of Dubertret includes a means for producing a mechanical property (specifically, conformational changes that inherently lead to increased flexibility of the hybrid assembly upon binding to a provided target; see paragraph 38) that provides information about the physical property of the nucleic acid polymer, specifically its hybridization state.

8. Claims 32-36, and 38-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Tomalia et al. (USPN 5,714,166).

Regarding claim 32, Tomalia teaches a dendrimer-nucleic acid-energy detector complex (column 1, line 66 – column 2, line 9) comprising a nucleic acid sequence and a dendrimer (column 2, lines 10-26). Tomalia also teaches that the dendrimer-nucleic acid complex may further include a signal generator, such as a fluorescent, bioluminescent, or phosphorescent entity, a signal reflector, such as a paramagnetic entity, or a signal absorber, such as a dye (column 16, line 56-column 17, line 33), all of which are energy detection devices.

Regarding claims 33 and 36, Tomalia teaches that the dendrimer comprises a conductive material, specifically metalloids (column 12, lines 42-45).

Regarding claim 34, Tomalia teaches that the dendrimer has a star shape, a starburst shape (Figure 1; column 1, lines 45-50), a spherical shape, or rod shape (column 12, lines 1-10).

Regarding claim 35, Tomalia teaches that the energy detection device is a fluorophore or chromophore (column 16, line 56 – column 17, line 33; see especially column 16, lines 59-62).

Regarding claim 38, Tomalia teaches that the complex is incorporated into an encapsulating agent (column 28, lines 53-63).

Regarding claims 39-41, Tomalia teaches transfection of the complex into a cultured cell (see column 41, lines 18-23 and also Example 70, column 120, lines 33-52) or administration to a multi-cellular organism (column 40, lines 35-46).

Regarding claims 42-45, Tomalia teaches that the nucleic acid may be DNA (single or double-stranded), RNA (which is a single stranded nucleic acid) (column 2, lines 16-27).

9. Claims 32-37 and 39-46 are rejected under 35 U.S.C. 102(e) as being anticipated by Tomalia et al. (USPN 6,475,994 B2).

Regarding claim 32, Tomalia teaches a dendrimer-nucleic acid-energy detector complex (column 2, lines 19-24) comprising a nucleic acid sequence (column 3, lines 1-7), a dendrimer (column 3, lines 9-10), and an energy detector (column 2, line 21 and lines 38-41; where the metals are energy detectors).

Regarding claims 33 and 36, the dendrimer of Tomalia comprises a conductive polymer, specifically a metal, such as gold or copper (column 2, lines 38-41).

Regarding claim 34, Tomalia teaches that the dendrimer may have a spherical or rod shape (column 4, line 67 – column 5, line 1). Tomalia also teaches the use of star shaped dendrimers (column 6, line 15).

Regarding claim 35, the conductive gold metal component of the dendrimer complex taught by Tomalia is inherently capable of transmitting and receiving energy. Therefore, this energy detection device may function as a transceiver.

Regarding claim 37, Tomalia teaches that the dendrimer polymer may be coated with gold nanoparticles (column 8, lines 44-52; where the gold particles in the gold sol are nanoparticles since their maximum dimension may be from 1-100 nm).

Regarding claims 39-41, Tomalia teaches transfection of the complex into cultured cells or administration to a multi-cellular organism (column 8, line 59 – column 9, line 3).

Regarding claims 42-46, Tomalia teaches that the nucleic acid may be DNA (a double-stranded nucleic acid), RNA (which is a single stranded nucleic acid), or cDNA (column 3, lines 1-8).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 2 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger et al. (USPN 6,443,898 B1) in view of either of Mirkin et al. (Nature, 1996) or Dubertret et al. (US 2004/0002809 A1).

Unger teaches therapeutic delivery systems comprising a lipid-encapusulated target agent (including nucleic acids) (see abstract and column 25, lines 42-52). Unger further teaches the inclusion of nanoparticles with the encapsulated therapeutic agent (column 23, lines 33-40).

Regarding claim 2, Unger teaches the application of ultrasonic energy to the therapeutic delivery system to release the contents of the liposome (column 28, lines 35-38; see also column 31, line 58 – column 32, line 3).

Regarding claims 6-8, Unger teaches transfection into cultured cells (column 33, lines 38-42) and also administration to multi-cellular organisms (column 33, lines 43-53).

Unger does not explicitly teach that the therapeutic agent (antisense nucleic acid) is conjugated to the nanoparticles.

Mirkin and Dubertret separately teach the device of claim 1, as discussed above.

Neither Mirkin nor Dubertret teach application of ultrasonic energy to the nanoparticle conjugate or transfection of the device into a cell.

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to incorporate the oligonucleotide-nanoparticle assemblies taught by either Mirkin or Dubertret into the therapeutic delivery systems of Unger in order to improve the detection capability of the system. Unger teaches monitoring the efficacy of the therapy solely through the use of ultrasound (see for example, column 4, lines 48-51). Mirkin and Dubertret separately taught visual (colorimetric) detection of nanoparticle-oligonculeotide conjugates where the detectable signal resulted from hybridization to a complementary nucleic acid (see page 608 of Mirkin and paragraphs 17 and 38 of Dubertret). The person of ordinary skill would have been motivated to utilize these directly detectable nanoparticle-nucleic acid conjugates to quickly and easily monitor their binding to target nucleic acids. The person of ordinary skill would have been particularly motivated to use the oligonucleotide-nanoparticle conjugates of Mirkin or Dubertret in the critical early-stage in vitro cell transfection studies proposed by Unger (column 33, lines 38-42), because doing so would have provided a rapid and direct method of detecting binding between the released oligonucleotide-nanoparticle conjugates the target nucleic acid, thereby minimizing the time required for screening multiple targets and reaction conditions. Therefore, the person of ordinary skill, interested in rapidly and easily detecting binding between a potential therapeutic nucleic acid and its target, would have been motivated to use the directly detectable oligonucleotide-nanoparticle conjugates taught by either Mirkin or Dubertret, thus resulting in the instantly claimed invention.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Torimoto et al. (Journal of Physical Chemistry B (1999) 42(103): 8799-8803) and Coffert et al. (Nanotechnology (1992) 3:69-76) teach attachment of multiple CdS nanoparticles to an immobilized DNA molecule. Baker et al. (USPN 6,471,968 B1) also teaches nucleic acid-dendrimer-energy detection devices.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela Bertagna whose telephone number is (571) 272-8291. The examiner can normally be reached on M-F 7:30-5 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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